

## PRELIMINARY AND SHORT REPORTS

## ACUTE URTICARIA FOLLOWING PYRIBENZAMINE THERAPY\*

## A CASE REPORT

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The recorded reports of cutaneous eruptions due to the antihistaminic drugs have been few in number (1, 2, 3, 4, 5, 6, 7), but none of these has been truly urticarial in nature. McElin and Horton (1) in 1945 reported one instance of generalized pruritus, following thirty-eight intravenous injections of Benadryl hydrochloride in twenty-six patients. Epstein (2) reported two patients with atopic eczema who developed eruptions while they were taking Pyribenzamine. Both eruptions cleared when the drug was discontinued, and recurred when it was readministered. Harris and Shure (3) reported an eczematoid dermatitis due to the ingestion of Pyribenzamine by a patient with allergic rhinitis. The eruption recurred following an additional dose of Pyribenzamine. Rattner and Graffin (4) reported a patient with a dermatitis medicamentosa due to gold therapy, who developed an exacerbation after taking Pyribenzamine orally. Sulzberger, Baer and Levin (5) reported two instances of contact dermatitis which developed following the use of Pyribenzamine ointment in ninety cases. Another similar case was reported by Strauss (6), whose patient showed a positive patch reaction to Pyribenzamine ointment and a negative reaction to the ointment base. Epstein (7) recently reported a patient with a generalized eruption, which appeared following Trimeton for a dermatitis of the vulval and anal areas. This eruption was at first urticarial in nature but later developed into a generalized maculo-papular eruption.

In the aforementioned instances of eruptions following the administration of antihistaminic drugs, these developed as a result of the treatment of either a preceding atopic eczema or some other allergic disease. The case described in this report is unique not only because it presented a true urticaria, but also in that no preceding eruption was present, nor was there any allergic history in the patient or his family. This patient developed a typical urticaria following the oral administration of Pyribenzamine.

## REPORT OF CASE

H. K., a white medical student, age 23, ingested one 50 mg. tablet of Pyribenzamine for coryza on October 8, 1948. Forty-five minutes later his face began itching and felt hot and flushed. Shortly thereafter, an urticarial eruption appeared over his face, associated with swelling of the eyelids. He was seen by one of us (M. M.) within an hour after taking the tablet, and a diffuse urticarial eruption was noted on the face, chest, abdomen, back and extremities. A minimal degree of pruritus was noted by the patient. He was given 0.5 cc of a 1:1000 solution of epinephrine hydrochloride subcutaneously, and the eruption disappeared within an hour.

This patient stated that he had never taken Pyribenzamine or any other similar antihistaminic agent prior to the initial dose which produced the eruption. He had never had any urticaria in the past, nor any other allergic disease.

As a test, on October 15, 1948, he was given one 50 mg. capsule of Benadryl hydrochloride. No reaction was noted. On October 23, a patch test was performed, using a small amount of a pulverized tablet of Pyribenzamine moistened with water. No reaction developed in forty-eight hours. On October 27, 1948, he took orally one 50 mg. tablet of Pyribenzamine. As nothing abnormal developed in forty-five minutes, he took another tablet.

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One hour following this, he noticed itching of both cheeks. Fifteen minutes later, on examination, there were noticed edema of the eyelids, and a diffuse, pruritic, urticarial eruption on the cheeks, chest, abdomen, back and upper extremities. These were in the form of wheals, 0.5 to 2 centimeters in diameter. Some coalescence of the wheals on the upper back was noted. Redness of the shaft of the penis, and a few wheals were present on the buttocks and thighs, but none on the legs or scrotum. He was given 0.5 cc of a 1:1000 solution of epinephrine hydrochloride, and again the eruption promptly disappeared.

This patient was tested with an oral dose of the excipient of the Pyribenzamine tablets.<sup>1</sup> He developed no eruption following this.

#### COMMENT

Pyribenzamine and the other antihistaminic agents are commonly used to combat acute urticarial eruptions, and one of their best known and most efficacious actions has been noted in this condition. The development of acute urticaria following the oral administration of Pyribenzamine is difficult to explain, if one accepts the theory that histamine or histamine-like substances produce urticaria, and that Pyribenzamine counteracts the action of histamine. Ratner (8), among others, contends that these drugs have not been proven to be antihistaminic, either chemically or pharmacologically, and adds that "the release of histamine has not yet been proved to be the fundamental factor in anaphylaxis or allergic reactions". Epstein (7) also questions the fact that histamine is really the cause of the cutaneous manifestations of dermatitis medicamentosa and eczematoid eruptions. Perhaps future knowledge of the significance of the spreading factor, hyaluronidase, may shed some light on the mechanism of allergic skin diseases. Mayer and Kull (9) have recently shown that Pyribenzamine counteracts the spreading effect of India ink and hyaluronidase, as well as counteracting the latter's effect of increasing the intensity of allergic skin inflammations.

It is interesting that this patient had only mild and transitory itching accompanying a rather severe urticaria. It has been noted (10) that the symptom of itching is relieved more consistently and more completely than the edema of urticaria in patients treated with the antihistaminic drugs. Perhaps this can be explained on the basis of the local anesthetic action of these drugs.

#### SUMMARY

Acute urticaria following oral administration of Pyribenzamine is reported in a person who gave no history of having taken this drug previously, or having had an urticarial eruption. The urticaria promptly disappeared following administration of epinephrine hydrochloride. Subsequent administration of Benadryl did not produce the urticaria. A patch test with Pyribenzamine was negative. Readministration orally of Pyribenzamine produced a recurrence of urticaria. The eruption did not recur following the oral ingestion of the excipient used in the tablets of Pyribenzamine. This indicates that the eruption was due to Pyribenzamine alone. No previous report of a similar case has been found by the authors.

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<sup>1</sup> Especially provided by the Ciba Pharm. Prod. Inc., Summit, N. J.

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